FIGURE 1

FIGURE 2

FIGURE 3

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601-1-098
Cip

C. elegans
eEF-2 kinase

Mammalian
eEF-2 kinase

MHCK A

FIGURE 4

I

H. EF2K	124
C.e. EF2K	110
MHCK A	572
MHCK B	132
MHCK C	48
heart K	189
melano K	48
ch 4 K	1127
consensus	

II

III

H. EF2K	178
C.e. EF2K	162
MHCK A	653
MHCK B	177
MHCK C	89
heart K	249
melano K	108
ch 4 K	1173
consensus	

IV

V

VI

H.EF2K	252
C.e. EF2K	235
MHCK A	734
MHCK B	254
MHCK C	165
heart K	335
melano K	189
ch 4 K	1253
consensus	

VII

VIII

FIGURE 5A

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LNNLHSHFILVDDGTVGKYGAEVRLRRELEKTINQQRIHARIGQGVPVVALIFEGGPNVIL
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EGKKKRTKDEIVDIDDPETKRFPYPLNELLIWACLMKRQVMARFLWQHGEESMAKALV
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EIQMKSKKLPITRKFYAFYHAPIVKFWFNTLAYLGFLMLYTFVVLVQMEQLPSVQEWIVI
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YDNHVFVAGRLIYCLNIIFWYVRLLDFLAVNQQAGPYVMMIGKMVANMFYIVVIMALV
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GSEERIRVTFERVEQMCIQIKEVGDRVNYIKRSLQSLDSQIGHLQDLSALTVDTLKTLTAQ
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EMGGGLRRAVKVQCTWSEHDILKSGHLYIIKSFLPEVVNTWSSIYKEDTVLHLCLREIQQ
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RKYNNNNGDEIIPTNTLEEIMLAFSHWTYEYTRGELLVLDLQGGVGENLTDPSVIKAEEKR
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PGNSTKESESTNSVRLML

Figure 7B

Figure 8A

ESAEPPLTQSDKRETSHTTAAATGRSSHADARECAISTQAEQEAKTLQTSTDSVSKEGNTNCKGEGMQVN
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KPCTCGPQQEEKQDRDGNIPDNFREDLKYEQSISEANDETMSPGVFSRHLPKDARADFREPVAVSVASPEP
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LCSSNDKTLEVFFQTQVSETSVSTCKSSKDGNSVMSPLFISTFTLNISHTASEGATGENLAKVEKSTYPLAS
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AKTLAFISGERELEKAPKLLQDPCQKGTLGCAKKSREREKSLEARAGKSPGTLTAVTGSEEVKRKPEAPGS
GHLAEGVKKKILSRVAALRLKLEKENIRKNSAFLKKMPKLETSLSHTEEKQDPKKPSCKREGRAPVLLK
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PLEGFGEVPEIIPIFLIHRPENNIPYATVEEELIGEFVKYSIRDGKEINFLRRESEAGQKCCTFQHWVYQKTSG
CLLVTDMQGVGMKLTDVGIATLAKGYKGFKGNCSMTFIDQFKALHQCNKYCKMLGLKSLQNNNQKQK
QPSIGKSKVQTNSMTVKKAGPETPGEKKT

Figure 8B

```
   1    atgtcccaga aatcctggat taaaggagta tttgacaaga gagaatgtag cacaatcata
  61    cccagctcaa aaaatcctca cagatgtact ccagtatgcc aagtctgcca gaatttaatc
 121    aggtgttact gtggccgact gattggagac catgctggga tagattattc ctggaccatc
 181    tcagctgcca agggtaaaga aagtgaacaa tggtctgttg aaaagcacac aacgaaaagc
 241    ccaacagata cttttggcac gattaatttc caagatggag agcacaccca tcatgccaag
 301    tatattagaa cttcttatga tacaaaactg gatcatctgt tacatttaat gttgaaagag
 361    tggaaaatgg aactgcccaa gcttgtgatc tcagtccatg ggggcatcca gaactttact
 421    atgccctcta aatttaaaga gattttcagc caaggtttgg ttaaagctgc agagacaaca
 481    ggagcgtgga taataactga aggcatcaat acagtgtcca agcatgttgg ggatgccttg
 541    aaatcccatt cctctcattc cttgagaaaa atctggacag ttggaatccc tccttggggt
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 661    gataacccc tcagcaagct cacaacactc aacagcatgc actcgcactt catcctgtct
 721    gatgatggga ccgtgggcaa gtatggaaat gaaatgaagc tcagaaggaa cctggagaag
 781    tacctctctc tgcagaaaat acactgccgc tcaagacaag gcgtgccggt cgtggggctg
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1141    ctggacttag caatcctaac agctttgctg aagggcacaa atttatcagc gtcagagcaa
1201    ttaaatctgg caatggcttg ggacagggtg gacattgcca agaaacatat cctaatttat
1261    gaacaacact ggaagcctga tgccctggaa caagcaatgt cagatgcttt agtgatggat
1321    cgggtggatt ttgtgaagct cttaatagaa tatggagtga acctccatcg ctttcttacc
1381    atccctcgac tggaagagct ctacaataca aaacaaggac ctactaatac actcttgcat
1441    catctcgtcc aagatgtgaa acagcatacc cttctttcag gctaccgaat aaccttgatt
1501    gacattggat tagtagtaga ataccteatt ggtagagcat atcgcagcaa ctacactaga
1561    aaaacatttca gagccctcta caacaacctc tacagaaaat acaagcacca gagacactcc
1621    tcaggaaata gaaatgagtc tgcagaaagt acgctgcact cccagttcat tagaactgca
1681    cagccataca aattcaagga aaagtctata gtccttcata aatcaaggaa gaagtcaaaa
1741    gaacaaaatg tatcagatga ccctgagtct actggctttc tttacccctta caatgacctg
1801    ctggtttggg ctgtgctgat gaaaaggcag aagatggcta tgttcttctg gcagcatgga
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2041    atgacgctgt tgacgtatga actcaggaac tggagcaatt cgacctgcct taaactggcc
2101    gtgtcgggag gattacgacc ctttgtttca catacttgta cccagatgct actgacagac
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2221    attttaccac ccaccatttt gacactggaa tttaaaagca aagctgagat gtcacatgtt
2281    ccccagtccc aggacttcca atttatgtgg tattacagtg accagaaccgc cagcagttcc
2341    aaagaaagtg cttctgtgaa agagtatgat ttggaaaggg gccatgatga gaaactggat
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2461    tatgagttct acagtgctcc aattgtcaag ttttggtttt atacgatggc gtatttggca
2521    ttcctcatgc tgttcactta caccgtgttg gtggagatgc agcccccagcc cagcgtgcag
2581    gagtggcttg ttagcattta catcttcacc aatgctattg aggtggtcag ggaggtgagt
2641    atttcagaac ctgggaagtt tacccaaaag gtgaaggtat ggattagtga gtactggaac
2701    ttaacagaaa ctgtggccat tggcctgttt tcagctggct tcgtccttcg atggggtgac
2761    cctccttttc acacagcggg aagactgatc tactgcatag acatcatatt ctggttctca
2821    cggctcctgg acttctttgc tgtgaatcaa catgcaggtc catatgtgac catgattgca
2881    aaaatgacag caaacatgtt ctatattgtg atcatcatgg ccatagtcct gctgagcttt
2941    ggagtggcac gcaaggccat cctttcgcca aaagagccac catcttggag tctagctcga
3001    gatattgtat ttgagccata ctggatgata tacggagaag tctatgctgg agaaaatagat
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3181    gtttacttag atatggaatc catttcaaat aacctgtgga aatacaaccg ctatcgctac
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3301    ggccttctcc tccgccgcct gtgctgtcat cgagctcctc acgaccaaga agagggtgac
3361    gttggattaa aactctacct cagtaaggag gatctgaaaa aacttcatga ttttgaggag
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3481    cgaatccgag tgacatcaga aagggttaca gagatgtact tccagctgaa agaaatgaat
3541    gaaaaggtgt cttttataaa ggactcctta ctgtctttgg acagccaggt gggacacctg
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3721    agctggagca atgtcatctg tgcagaggtt ctaggcagca tggagatcgc tggagagaag
3781    aaataccagt attatagcat gccctcttct ttgctgagga gcctggctgg aggccggcat
3841    ccccccaagag tgcagagggg ggcacttctt gagattacaa acagtaaaag agaggctaca
3901    aatgtaagaa atgaccagga aaggcaagaa acacaaagta gtatagtggt ttctggggtg
3961    tctcctaaca ggcaagcaca ctcaaagtat ggccagtttc ttctggtccc ctctaatcta
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Figure 9A

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4021   aagcgagttc cttttcagc agaaactgtc ttgcctctgt ccagaccctc tgtgccagat
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4141   ccagttgtct ctgactgggc atcagtggat gaacccaagg aaaagcacga gcctattgct
4201   cacttactgg atggacaaga caaggcagag caagtgctac ccactttgag ttgcacacct
4261   gaacccatga caatgagctc ccctctttcc caagccaaga tcatgcaaac tggaggtgga
4321   tatgtaaact gggcattttc agaaggtgat gaaactggtg tgtttagcat caagaaaaag
4381   tggcaaacct gcttgccctc cacttgtgac agtgattcct ctcggagtga acagcaccag
4441   aagcaggccc aggacagctc cctatctgat aactcaacaa gatcggccca gagtagtgaa
4501   tgctcagagg tgggaccatg gcttcagcca aacacatcct tttggatcaa tcctctccgc
4561   agatacaggc ccttcgctag gagtcatagt tttagattcc ataaggagga gaaattgatg
4621   aagatctgta agattaaaaa tctttcaggc tcttcagaaa tagggcaggg agcatgggtc
4681   aaagcgaaaa tgctaaccaa agacaggaga ctgtcaaaga aaaagaagaa tactcaagga
4741   ctccaggtgc aatcataac agtcaatgcc tgctctcaga gtgaccagtt gaatccagag
4801   ccaggagaaa acagcatctc tgaagaggag tacagcaaga actggttcac agtgtccaaa
4861   tttagtcaca caggtgtaga accttacata catcagaaaa tgaaaactaa agaaattgga
4921   caatgtgcta tacaaatcag tgattaccta aagcagtctc aagaggatct cagcaaaaac
4981   tctttgtgga attccaggag caccaacctc aataggaact ccctgctgaa aagttcaatt
5041   ggagttgaca agatctcagc ctccttaaaa agccctcaag agcctcacca tcattattca
5101   gccattgaaa ggaataattt aatgaggctt tctcagacca taccattttac accagtccaa
5161   ctgtttgcag gagaagaaat aactgctac aggttggagg agagttcccc tttaaacctt
5221   gataaaagca tgtcctcttg gtctcagcgt gggagagcgg caatgatcca ggtattgtcc
5281   cgagaggaga tggatggggg cctccgtaaa gctatgagag tcgtcagcac ttggtctgag
5341   gatgacattc tcaagccggg acaagtttc attgtcaagt cctttcttcc tgaggttgtg
5401   cggacatggc ataaaatctt ccaggagagc actgtgcttc atctttgcct cagggaaatt
5461   caacaacaaa gagctgctca aaaattgatc tataccttca accaagtgaa accacaaacc
5521   ataccctaca caccaaggtt cctggaagtt ttcttaatct actgccattc agccaaccag
5581   tggttgacca ttgagaagta tatgacaggg gagttccgga agtataacaa caacaatggt
5641   gatgaaatca cccccaccaa caccctggag gagctgatgt tggctttctc tcactggacc
5701   tatgagtaca ctcgggggaga gctgctggtt ttagatttgc aaggtgttgg agaaaatttg
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6361   aggatggggt tgggggggat acatttattt tattttctca ctatgtatgc agactggacc
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6481   aaaagttatg tgatttcctc ctctgtcttt tccacaacat aggactttga atagcaatga
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6661   cctggatatt tcaggtttct gtaaaagaaa gggaaaccta aaacaaatac ccttccatat
6721   ataatatata tggaatatgt atattatata tattttata tatataatat atatggaata
6781   tatatattat atatataaaa tacatatgga atatatatat tttatatata tatatatatt
6841   tttattttttg agatggagtt tcactctttt tacccaggct ggagtgcaat gatgcgatct
6901   cactgcaacc tctgcctccc gggcttgagc gattcttgtg tctcagtctt ccgggtagct
6961   gggactacag gtgtgcacca ctatgcctgg ctaatttttgt attttagta gagatggggt
7021   ttcaccatgt tggccaggct ggtctcaaac tcctgacctc agatgatcca cctgccttgg
7081   cttcccaaag tgctgggatt acaggcgtga gccactgcgc ctgcccttt ttttttttt
7141   tttaaacgag aacaagaata tgaagaactg gaaatcatta agaaagggtt tcccttcctt
7201   aaagctcagg ggtactatta gttaggagtt gactaactca acctgtaaaa caccactcct
7261   ccttccaaag ttgtatatat aatattgcag gttaaattac tttatgtcag gtcctatgaa
7321   gaaagatacg gtttcagact gaaaacatgt ttcacaggtg tttgcttcct tccagagcag
7381   agttccctat tcccctggca taaagaatgt atatatattt tgaaatatgg ctgagaacat
7441   gtcattggtt tgtgaggcct aaggtgaagc actcctggca gccacactgt gtagtgtatt
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7561   agcttttcac acaaggagag atgtgggggct gggagtcctc tccccatcct attgcatctc
7621   ctttcttatt ataagctgtt ccagttcaca ggcagcaaac ctcctgggtt tgaaaaattc
7681   caacttattt ttatctttaa tcctgacatt agctgacttg ctagtgagct tgctttaaaa
7741   atctcacactc ttgcattctt aggcatacag gggaaatgtt gaaaaggaag gtggaaaacc
7801   aagaatttag tttgccaatg attgcctctg attcttgtaa gtttgagttc cacaagggct
7861   aatttattcc cctttacttt gggttttggg gtggtgaaa gcggaaatt tgggtgattt
7921   gttgattggc aatgaggata aaatgttaat actttttggg ggactaaca actttatcct
7981   attctacaag tcagtaaagg aacaattggt actcacctca gtgctgcact caactatgga
```

Figure 9A

8041   aagaggcaga gtttgcttgc ccaattgcca aactaaagac atcagttcat tggtcaaata
8101   tttgttacct ggaatggaac ttgaaagcaa atacatttgg attcaaatt tcaaaaaa

Figure 9A

Human kidney kinase

MSQKSWIKGVFDKRECSTIIPSSKNPHRCTPVCQVCQNLIRCYCGRLIGDHAGIDYSWTIS
AAKGKESEQWSVEKHTTKSPTDTFGTINFQDGEHTHHAKYIRTSYDTKLDHLLHLMLKE
WKMELPKLVISVHGGIQNFTMPSKFKEIFSQGLVKAAETTGAWIITEGINTVSKHVGDAL
KSHSSHSLRKIWTVGIPPWGVIENQRDLIGKDVVCLYQTLDNPLSKLTTLNSMHSHFILS
DDGTVGKYGNEMKLRRNLEKYLSLQKIHCRSRQGVPVVGLVVEGGPNVILSVWETVKD
KDPVVVCEGTGRAADLLAFTHKHLADEGMLRPQVKEEIICMIQNTFNFSLKQSKHLFQIL
MECMVHRDCITIFDADSEEQQDLDLAILTALLKGTNLSASEQLNLAMAWDRVDIAKKHI
LIYEQHWKPDALEQAMSDALVMDRVDFVKLLIEYGVNLHRFLTIPRLEELYNTKQGPTN
TLLHHLVQDVKQHTLLSGYRITLIDIGLVVEYLIGRAYRSNYTRKHFRALYNNLYRKYK
HQRHSSGNRNESAESTLHSQFIRTAQPYKFKEKSIVLHKSRKKSKEQNVSDDPESTGFLY
PYNDLLVWAVLMKRQKMAMFFWQHGEEATVKAVIACILYRAMAHEAKESHMVDDAS
EELKNYSKQFGQLALDLLEKAFKQNERMAMTLLTYELRNWSNSTCLKLAVSGGLRPFV
SHTCTQMLLTDMWMGRLKMRKNSWLKIISIILPPTILTLEFKSKAEMSHVPQSQDFQFM
WYYSDQNASSSKESASVKEYDLERGHDEKLDENQHFGLESGHQHLPWTRKVYEFYSAP
IVKFWFYTMAYLAFLMLFTYTVLVEMQPQPSVQEWLVSIYIFTNAIEVVREVSISEPGKF
TQKVKVWISEYWNLTETVAIGLFSAGFVLRWGDPPFHTAGRLIYCIDIIFWFSRLLDFFA
VNQHAGPYVTMIAKMTANMFYIVIIMAIVLLSFGVARKAILSPKEPPSWSLARDIVFEPY
WMIYGEVYAGEIDVCSSQPSCPPGSFLTPFLQAVYLFVQYIIMVNLLIAFFNNVYLDMESI
SNNLWKYNRYRYIMTYHEKPWLPPPLILLSHVGLLLRRLCCHRAPHDQEEGDVGLKLY
LSKEDLKKLHDFEEQCVEKYFHEKMEDVNCSCEERIRVTSERVTEMYFQLKEMNEKVS
FIKDSLLSLDSQVGHLQDLSALTVDTLKVLSAVDTLQEDEALLAKRKHSTCKKLPHSWS
NVICAEVLGSMEIAGEKKYQYYSMPSSLLRSLAGGRHPPRVQRGALLEITNSKREATNV
RNDQERQETQSSIVVSGVSPNRQAHSKYGQFLLVPSNLKRVPFSAETVLPLSRPSVPDVL
ATEQDIQTEVLVHLTGQTPVVSDWASVDEPKEKHEPIAHLLDGQDKAEQVLPTLSCTPE
PMTMSSPLSQAKIMQTGGGYVNWAFSEGDETGVFSIKKKWQTCLPSTCDSDSSRSEQHQ
KQAQDSSLSDNSTRSAQSSECSEVGPWLQPNTSFWINPLRRYRPFARSHSFRFHKEEKLM
KICKIKNLSGSSEIGQGAWVKAKMLTKDRRLSKKKKNTQGLQVPIITVNACSQSDQLNP
EPGENSISEEEYSKNWFTVSKFSHTGVEPYIHQKMKTKEIGQCAIQISDYLKQSQEDLSKN
SLWNSRSTNLNRNSLLKSSIGVDKISASLKSPQEPHHHYSAIERNNLMRLSQTIPFTPVQL
FAGEEITVYRLEESSPLNLDKSMSSWSQRGRAAMIQVLSREEMDGGLRKAMRVVSTWS
EDDILKPGQVFIVKSFLPEVVRTWHKIFQESTVLHLCLREIQQQRAAQKLIYTFNQVKPQ
TIPYTPRFLEVFLIYCHSANQWLTIEKYMTGEFRKYNNNGDEITPTNTLEELMLAFSHW
TYEYTRGELLVLDLQGVGENLTDPSVIKPEVKQSRGMVFGPANLGEDAIRNFIAKHHCN
SCCRKLKLPDLKRNDYSPERINSTFGLEIKIESAEEPPARETGRNSPEDDMQL

Figure 9B

GTATCAGGACTCAGCCCATTCCCCTCTGGTGTCTGCTGAGAAATGGAGGCCGAAGGAGGAGTGATCTAGAAGTGTTAATTGAGCCCTAATCTATGCTAGTTACTGGGGG
TGTTGGGGGGAGACAGGAGAGAGATCCCACGGGGTTCCGGCCTCCAGGACTCAGTCACTAATGGAGGTGGCTTGGCTTGTCTATGTGCTGGCAACAGCCA
CTGGGCGAGGCAAGGCGAGGTCAGTCACGGCTGGTCCCGGAAGGAGGGCTGGTTCTTTGGCTCCCGGGTCTTCCCCGGTCTCAGCCAAGCTGGCCAGCGGTTGAC
CTGCTCCCCTGGCCCCGGCCTGGTCGTGACCCCCCATATGCCACACGGACATGAGCAGGCCGGACGCGGCGGTCCCGGGAGCTCCAGGAGCGGACT
TGTCCTCCATGACCAGGACACCGGCCTCCTGCGCCTTCCTCCCGAGCCGGCTCCCAGCCGCCGGTTCCAGCCCGGGTCGGGCAGGGAGGGAGGCAGCAGCAGGTG
CGGAGCCGGCCCCGGCCCTGGGCGGGGCCACCGGCTATAAATAGGGCGCGGTCAGCCGCGGTGCCATGGCGGTGGGGAGGGCGGTGCCCAGCCGCTCACCCGGAGGACAGC
ACGACGGCCCGGCCACCGGCTATAAATAGGGCGCGGTCAGCCGCGGTGCCATGGCGGTGGGGAGGGCGGTGCCCAGCCGCTCACCCGGAGGACAGC
GAGGCAGCGGCGAGGTGCGGGGCGGCGGACGACGCCCGTGTGATCCCGAGCCAGCTCACAGTTTCGTCTCCATCATTGCTCTCCATCAGGATACCCAGCTGTAAGTTGCCGAGACCCAGCTTATCAAGCAACCGGTT
GTCTCACCCCAGCTCTGGAAGGAGCACGTTCACCTGCATGGTCAGCTGCAATTGCTCCAGCTGTTGGGCACCGTCTGCTCCAGACGTGTCTGCCCGAGACCCAGCTGTAAGTTGCCGAGACCCAGCTTATCAAGCAACCGGTT
GAGGACAGCAGCGACGTCAGGTTCACCTGCATGGTCAGCTGCAATTGCTCCAGCTGTTGGGCACCGTCTGCTCCAGACGTGTCTGCCCGAGACCCAGCTGTAAGTTGCCGAGACCCAGCTTATCAAGCAACCGGTT
AAATATGAGATCACTCATCAGGGTGCAATTGCTCCAGCTGTTGGGCACCGTCTGCTCCAGACGTGTCTGCCCGAGACCCAGCTGTAAGTTGCCGAGACCCAGCTTATCAAGCAACCGGTT
GCATTGTGTCCTGTCTCAGGGGTCGGGCAATTGCTCCAGCTGTTGGGCACCGTCTGCTCCAGACGTGTCTGCCCGAGACCCAGCTGTAAGTTGCCGAGACCCAGCTTATCAAGCAACCGGTT

Figure 10A

GGCCCGGAGGAAGAGATTTCTCCCTAAGGTCAGAGCAGCAGGAGGACGGGGAGGCAACCACACCTGAAGAAAAGGGAGGAGCCCACGGTTTCCCCCGGGGGCCC
AGGAAAAGCCTGGTCGTGCCTGGGTCCCCAGGGACTCCAGGGGTGGGGAGAGACGCTCCCCTACGCAGGGCAGGGCAGAAAGGGCGAGCATGCTGGAGGTGCTCGGGCAGAGG
AGGAGCTGGCGGCAGGAGGACCTGGCCCCAGCCTGGCCCCACCAGGTCCGGAAGATTCGGGTGGAGCAGTTCCTGATGCCTCCGGTAGCCTGAAGCTGTGGTGCCAAGCCAG
GAAAGCCAAAGACCTGCTGAAAGCCCCACAGGTTGACATGGGCCAAGGATCAGCGCCGAGTGGGCAGAGTGGGCAGGGATGAGGGCCGGCGGCCTGGCCATCGTGC
CATTCTTAGTTGACTCAGTCTTGACATGGTGTGTATGGTGCACCATCCACAATGAGCACGGCTCGGCCTCGGCTGCTTGGCTAAGGGTCTGGCTGGCTGGCTGGGGGGACAAGCTCTTTGGGC
AGGCCTCCCCCGTAGACTGCGGTGTGTATGGTGCACCATCCACAATGAGCACGGCTCGGCCTCTGCCTCAGCCTGGCTGGTGTTGCAGGATTCAT
CTCCAGAGAAGAAGGTGAAGTTGGAGAGATTGAGATGACCCCTATGGTGTTTGCTAAGGGTCTGGCTGGCTGCTGGGGGGACAAGCTCTTTGGGC
GACTGGTAAGCGAGGAGCTCCGAGGGGTGGATATGGGTGTGCCTTCGGAAGGCCTCCCAGCAGTGAGACTTCTCTTGTGGGCAGAAACTACGACGTCACCATCCAGGGGTGCAAGATC
CGCACGTGCATCATCAAGGTGTCCAGCCTGCTGTGTTGGGCCCAGCAGTGAGACTTCTCTTGTGGGCAGAAACTACGACGTCACCATCCAGGGGTGCAAGATC
CAGAACATGAGTCGGGAGTACTGCAAAATCTTCGCAGCAGAAGCCCGGCGCGGCGGTGACCCTGTATCAGTGGACAAATGGCAGCTTCCTTGTCACAGACTTGGCAGGGGTTGACTGGAAG
CCTGCAAACAATATCCCATATGCTACCCTGGAGGAAGACCTGGCAAGCCCCTGGAGTCTACTGTTCTCGGAGGCTGTGCTGAGGCTCCGACAGCATCT
GGCAGCTCTGAGGCCATGCAGAAATGCCAGACCTTCCAACACTGGCTGTATCAGTGGACAAATGGCAGCTTCCTTGTCATCGTCTCCCACCAGTTGCAAT
ATGACTGATGTGCAGATTGCTACCAAACTCCGAGATACCCAGGGCCTCAAGGAAAGTGCTTCCTGCTGGACCCGGTTCGCTCTCTCCCACCAGTTGCAAT
GCCTACTGTGAGCTGCTGGGGCTGACACCTCTCAAGGCCTCTCCAGAAGAAAGGCTCTCCCTAGTCCTGACATGCGGATACCCAGGGCCCCAGGGAAGTGCTCCAACCCCTCAGCGCTCAGAGCCAGT
CACCACTCAGTTGTTGGGACAGCCTCCACCACCAAGAAAGGCTCCCAACCCAGAGAGAGGGCTCCAAGGGCCATGGAAGGTGCACGAAGGTGCACGAACTAACTGGAACCACCACTTGGGGACCTCTCTGAGCAGGCT
CCAACCAGGAAGCAGCTTGAACTGGATGGCATTTCCAAATATGGAACTAACTGGAACCACCACTTGGGGACCTCTCTGAGCAGGCT
CTCGTGAATCAGCTCGTCATCAGATGGCTTTGGTGCATGGAAGTTACACTTTGCCACTGCTGAGTTCTGCATGAGTTCTCACCCCAAGCCCTTGCC
ACCTCCGAGTGCCTGGCAACCTAGGCCCTTCCTTGAAGTTACACTTTGCCACTGCTGAGTTCTGCATGAGTTCTCACCCCAAGCCCTTGCC
CCAGCCCAGTCCAGCAGCAGATGTTACAATCTGAGTGAGGACATGCAGGCCAACTTTTACCCTCCTGATCTGCCTGTCCTGTCCTGTCCCGATCC
AGACTTCCTCTGCTGGTGCTGGTCCTCAGCCTGGTCATGTCCTGGACTCTCAGGGTATCTTCTCCTCCAGCTACTCCTTCCAGTGCAACTAACCATCCTTGAGCCC
CTTGTACCCCTGCCACATCCTTCCAGCCTGGACCCTGCGCAGCCTGTGCAGTGGCCTTGATGTCCTTGTGCAGGCCTTTGCTCACTCGCCTCTTCCCATGCTCCC
CCACCAATACCAGGTGAGGAACAGACCTGCGAGGCTGTAGCCAGGAGAGGGTGTGTCAGCTGTCATCCATGCACTTGGGTGGAGGCTGGTG
TGAGGGTTGTGTCAGCAGGCTCAGCAGAGGCCCATGGTGTCTAGCCAGGAGAGGGTGTGTCAGCTGTCATCCATGCACTTGGGTGGAGGGAGTCTCTGT
TCAACCAGGAGTGGAAGCTGACCCCTGCTCCACCATCGCTCTTGACTCTGGGTGTTCTCAGGTACTTGGGTGTGGTTCCCAGCCTGGATCCTTCC
GCCTGGGAATTAGGACCCCTGCTCCACCATCGCTCTTGACTCTGGGTAGGTCTGCAGCTACTCCCTTTGAATGCAATAAAGGCAGCATTGTGTGCCCTGCCCTCATCTGGT
AGAGCATCCCTCTGAGGGCTGGGATGGGGTAGGTCTGCAGCTACTCCCTTTGAATGCAATAAAGGCAGCATTGTGTGCCCTGCCCTCATCTGGT
GTGGTTGGAGGTCTGTGGAGTCAAGGTCCCCTCTGTGGCCACAGAAGAGAAGCACCCAGGAAGCAGAGCTGGGGGCTCTGGAAACGCCCTGTGTCTGGAC
TGGACCGAAGTTCAGTCGCAGCCTTCTGTGAATTGCTCTTCAGTAGAAGAGAACACAAAGGAAGCACCCAGGAAGCAGAGCTGGGGGCTCTGGAAACGCCCTGTGTCTGGAC
TTACGCCTTTGGAATTGCTCTTCAGTAGAAGAGAACACAAAGGAAGCACCCAGGAAGCTTTTCATTCCCACCCCACCC
TACAGCAAGACCAGCCAGGAGCCCACCAGCACCTGCCTTCAGACACTTGCTGACACTCTCTGACTTCTCTACCCTCTCTGTGCTCAGGTGACTCCACATCTTCTGCCCCAGTGTGTCCCCACC
CGGAACCTCCCAGCCTGGTATACCCAGATTACTTTGGTGAACTGAAAA
CTCTCCCAGCCTGTATACCCAGATTACTTTGGTGAACTGAAAA

MEVAWLVYVLGQQPLARQGEGEGQSRLVPGRGLVLWLPGLPRSSPSWPAVDLAPLAPARPRGPLICHTGHEQAGREPGPGSST
KGPVLHDQDTRCAFLPRPPGPLQTRRYCRHQGRQGSGLGAGPGAGTWAPAPPGVSKPRCPGRARPGEGQQQVTTARPPAIN
RGARQPRAGAAAAGRGPGAGAWRTGEAAASAGPAVGEGGAMGSRRAPTRGWGAGGRSGAGGDGEDDGPVWIPSASRS
YLLSVRPETSLSSNRLSHPSSGRSTFCSIIAQLTEETQPLFETTLKSRSVSEDSDVRFTCIVTGYPEPEVTWYKDDTELDRYCGL
PKYEITHQGNRHTLQLYRCREEDAAIYQASAQNSKGIVSCSGVLEVGTMTEYKIHQRWFAKLKRKAAAKLREIEQSWKHEK
AVPGEVDTLRKLSPDRFQRKRRLSGAQAPGPSVPTREPEGGTLAAWQEGETETAQHSGLGLINSFASGEVTTNGEAAPENGE
DGEHGLLTYICDAMELGPQRALKEESGAKKKKDEESKQGLRKPELEKAAQSRRSSENCIPSSDEPDSCGTQGPVGVEQVQT
QPRGRAARGPGSSGTDSTRKPASAVGTPDKAQKAPGPGPGQEVYFSLKDMYLENTQAVRPLGEGPQTLSVRAPGESPKGK
APLRARSEGVPGAPGQPTHSLTPQPTRPFNRKRFAPPKPKGEATTDSKPISSLSQAPECGAQSLGKAPPQASVQVPTPARRRH
GTRDSTLQGQAGHRTPGEVLECQTTAPTMSASSSSDVASIGVSTSGSQGIIEPMDMETQEDGRTSANQRTGSKKNVQADGK
IQVDGRTRGDGTQTAQRTRADRKTQVDAGTQESKRPQSDRSAQKGMMTQGRAETQLETTQAGEKIQEDRKAQADKGTQE
DRRMQGEKGMQGEKGTQSEGSAPTAMEGQSEQEVATSLGPPSRTPKLPPTAGPRAPLNIECFVQTPEGSCFPKKPGCLPRSEE
AVVTASRNHEQTVLGPLSGNLMLPAQPPHEGSVEQVGGERCRGPQSSGPVEAKQEDSPFQCPKEERPGGVPCMDQGGCPLA
GLSQEVPTMPSLPGTGLTASPKAGPCSTPTSQHGSTATFLPSEDQVLMSSAPTLHLGLGTPTQSHPPETMATSSEGACAQVPD
VEGRTPGPRSCDPGLIDSLKNYLLLLKLSSTETSGAGGESQVGAATGGLVPSATLTPTVEVAGLSPRTSRRILERVENNHLV
QSAQTLLLSPCTSRRLTGLLDREVQAGRQALAAARGSWGPGPSSLTVPAIVDEEDPGLASEGASEGEGEVSLEGPGLLGAS
QESSMAGRLGEAGGQAAPGQGPSAESIAQEPSQEEKFPGEALTGLPAATEEELALGARRKRFLPKVRAAGDGEATTPEERES
PTVSPRGPRKSLVPGSPGTPGRERRSPTQGRKASMLEVPRAEEELAAGDLGPSKAGGLDTEVALDEGKQETLAKPRKAKDL
LKAPQVIRKIRVEQFPDASGSLKIWCQFFNILSDSVLTWAKDQRPVGEVGRSAGDEGPAALAIVQASPVDCGVYRCTIHNEH
GSASTDFCLSPEVLSGFISREEGEVGEEIEMTPMVFAKGLADSGCWGDKLFGRLVSEELRGGGYGCGLRKASQAKVIYGLEPI
FESGRTCIIKVSSLLVFGPSSETSLVGRNYDVTIQGCKIQNMSREYCKIFAAEARAAPGFGEVPEIIPLYLIYRPANNIPYATLEE
DLGKPLESYCSREWGCAEAPTASGSSEAMQKCQTFQHWLYQWTNGSFLVTDLAGVDWKMTDVQIATKLRGYQGLKESCF
PALLDRFASSHQCNAYCELLGLTPLKGPEAAHPQAKAKGSKSPSAGRKGSQLSPQPQKKGLPSPQGTRKSAPSSKATPQASEP
VTTQLLGQPPTQEEGSKAQGMR

Figure 10B

ATGAATAATCAAAAAGTGGTAGCTGTGCTACTGCAAGAGTGCAAGCAAGTGCTGATCAGCTCTTGTTGGAAGCGCCAGATGTGTGGAAGAGAGGACAAGAGCGA
GGACCAGCGCTGCAGAGCTTTACTCCCCAGCGAGTTAAGGACCCTGATCAGGAGGCAAAGGAAATGAAGTGGCCCTTCGTGCCTGAAAAGTGGCAGTACAAAC
AAGCCGTGGGCCCAGAGGACAAAACCTGAAGGATGTGATTGGCGCCGGGTTGCAGCAGTTACTGGCGGTCCCTGAGGGCCTCCATCCTCGGTCTCGGGACTGT
GCGGCTGCGGCGGCTATTGTTCTTGGTGGACCGGTTCCTGTATGGGCTCGACGTCTCTGCAGGTCGCCAAAGGTCTCCAAGTTGCAGCCAG
CCACGCCAATTGCCCCGCAGGTGGTTATTCGGCCAAGCCGAATTCTCCGTGAACTCAGGAAAACTTTTAAAGCAGATGCAGTATATTCTGAGCAGTCTAATAAGCAACA
ATGGAGCAACGGGTACCTGGCTGTGTACAGAAATGAAAGTGACAAGGTCCTGGTCGCAGATCGGTCTCGTATACAGGGCAGATTCTGCAAAGCTGGGTATG
TGGTACGAAGCAGCAGAGTAATATGGGCCTCCATTGTAGGATATTTGGCACTTCCTCAGCCGGATAAAAAGGGCTGTGAAGGAGTTTGACCACCATTTGCTGTCCGCTGCAG
AAGCCTGCAAGCTGGCAGCTGCCTTCAGTTGCCTATACGCGCGTCTTCAGTTGCGTGTAATCCGTGCACGTGTTTATTGTCCTACAGTAGTTCAATGA
CTGTCCTCCAGAATTGAAAACTTACATCTGTGTGAAGCCAAAGAGCCTTTGAGATTGGCCTCCTCACCAGAGAGATGATGAGCCTGTTACTGGAAAACAGGA
GCTTCACAGCTTTGTCAAAGCTGCTTTCGGTCTACCACCAGAGTGCACACAGGGACACGGTCCATGGGGAGACAGGACGGTCCTCGAGGCAAGTTCTGTAGGAAGC
AATGGGGAAGCTGTACAATTCAGCACTTCCTCCAGAGTCAGGAGAAGCTCTGTCTCAAGAAGTTATGTCTGTGATTGCCCAGGTGGAACACATTTACA
AGTTCAAAGCTTCTCAAATGTAGATGACAGATCTTATCTTCCCGGAGTGTGCAGGTTGGATAAACTTATCTTGCATGGGCAAGGGGATTTCCAAAAAT
CCTTGACACCTATTCACAGCACCATACTTCGGTGTGTGAAGTATTTGAAGTGATTGTGGAAACAACAAAATGAACAGAAAAGATGCAAAAAGAGTCTGCA
TCACTGCTCTAAAAACAGAAATAAAAACATAGATACTGTGAGTACTACTCAAGAAAGCCACATTGTCAAAGAGACACAGGAATATCTTCCTCCTAATGGGT
AAGAATGTTCAGAGGAACTCAGAAGGGGGAGGCTGTTTTCAACAAGTCTCTGAGTGGCAGCCAGAACTTCAGGGTTTAGTTCCTCTGCAAG
CTGGGGAAGTGAATGGTCACGTTGACGACAGGTCAGCGACACTCGGTGGACACTCAGTGTCCACTGCCTTGTCTGTGGAGAC
TAGAATGACAGGGAAGGCAGAGCTATGCATTCATTGCATCATTGCCCTCATAATACCCCAGACCTCATATGTTGAATTCGGTGGCTTCTGAATTCGGTAGGCCTTCAAATC
AGCCACAGCAACAGATGCCCTTGACACCTGGTGGACACCAGAAATACTTCTGCTCACTCCAGACCCTCATATCGTTCTGTCTTGTCTGTTTCGATTCTGGTAGGCCCAAGAATATGGGCAC
AGGAAGTCAGAAATATGGGACCAGAAGAAGCCTTTGAAATAATGTTGAATTAATTGTGAAATAATGTGGAGTTTCAGAAACCAACTGCGATGTCAAAGGACAACAGCAGGGGAAAAGAGCACTGAAGATGCACCCTTAGACTTTCA
ATTAGTGAAAGAGAGGCGCAGCCTACACTTGGGAAACATTTCCATGCCTCCCTACCCCTAATTGGCCTGTTCAAAATCCTGACTCCAGAAAAAGTGGTGGCCCA
CAGGGTCCTGCACAATTCTCTGGGAAACATTTCCATGCCTCCCTGATGGGCCCTGATGGGCGGAGGGGCAACTGGGCCCCAAATGGCACGGGCTCTCATAG
GTCGCAGAGCAGGGCATGACACGCCGCTGAAATGTTCTGGGAGTTCTTCATTGCGGGGAAAAGATCCGGGAAGATGAGGAAAAGATCCCTGCACCTGA
ACTGTGCATTCTGAGACAGCGGTTCATCATCTTCATCAGAAGAGAAATTCTGGGGAGTATGTTGGGGAAGAAATTCTGTGAAGAAAAGGCAGACACAGTGC
TGCTTTTTGGGTTCATCATCTTCATCAGAAATCTGACAGATATGTTCTATAGAAGAGACTCTATGGAAGACTCCACCAATATCCACTACTGAT
TTTAGAGGACAAGAGACAATAAAGGGATGTATCAGTGTACCTATGGCCATTTTCTTATGAGTTTCTAAATCATAGATGATTGTTGGTCGATTTTACAAGGTTGGTGTCGATTTTACAAGATACA
AAGCCACAGAATATGGCTTGGCCTATGCCCAGATTCCCAGATTCACTCCGTTGATCAGAAAGTTTCACTACCACATTTGTCAAATAACAGAAGTGGTGAAAAACAGATTGGTGAAAACAGAATACA
ACTCATCTCACCTCACCTGACAGATCTGCCCATGTCTGCCCATGTCGTCTTTCTTTGACTAGACCTTCAATGGAGAAACCA
GAATGTAATGAAATCTGCCCATGTAAATCTGCCCATGTCGTCTTTCTTTGACTAGACCTTCAATGGAGAAACCA

Figure 11A

MNNQKVVAVLLQECKQVLDQLLEAPDVSEEDKSEDQRCRALLPSELRTLIQEAKEMKWPFVPEKWQY
KQAVGPEDKTNLKDVIGAGLQQLLASLRASILARDCAAAAIVFLVDRFLYGLDVSGKLLQVAKGLHKL
QPATPIAPQVVIRQARISVNSGKLLKAEYILSSLISNNGATGTWLYRNESDKVLVQSVCIQRGQILQKLGM
WYEAAAELIWASIVGYLALPQPDKKGLSTSLGILADIFVSMSKNDYEKFKNNPQINLSLLKEFDHHLLSAAE
ACKLAAAFSAYTPLFVLTAVNIRGTCLLSYSSSNDCPPELKNLHLCEAKEAFEIGLTKRDDEPVTGKQEL
HSFVKAAFGLTTVHRRLHGETGTVHAASQLCKEAMGKLYNFSTSSRSQDREALSQEVMSVIAQVKEHLQ
VQSFSNVDDRSYVPESFECRLDKLILHGQGDFQKILDTYSQHHTSVCEVFESDCGNNKNEQKDAKTGVCI
TALKTEIKNIDTVSTTQEKPHCQRDTGISSSLMGKNVQRELRRGGRRNWTHSDAFRVSLDQDVETETEPSD
YSNGEGAVFNKSLSGSQTSSAWSNLSGFSSSASWEEVNYHVDDRSARKEPGKEHLVDTQCSTALSEELEN
DREGRAMHSLHSQLHDLSLQEPNDNLEPSQNQPQQQMPLTPFSPHNTPGIFLAPGAGLLEGAPEGIQEVR
NMGPRNTSAHSRPSYRSASWSSDSGRPKNMGTHPSVQKEEAFEIIVEFPETNCDVKDRQGKEQGEEISERG
AGPTFKASPSWVDPEGETAESTEDAPLDFHRVLHNSLGNISMLPCSSFTPNWPVQNPDSRKSGGPVAEQGI
DPDASTVDEEGQLLDSMDVPCTNGHGSHRLCILRQPPGQRAETPNSSVSGNILFPVLSEDCTTEEGNQPG
NMLNCSQNSSSSSVVWLKSPAFSSGSSEGDSPWSYLNSSGSSWVSLPGKMRKEILEARTLQPDDFEKLLA
GVRHDWLFQRLENTGVFKPSQLHRAHSALLLKYSKKSELWTAQETIVYLGDYLTVKKGRQRNAFWVH
HLHQEEILGRYVGKDYKEQKGLWHHFTDVERQMTAQHYVTEFNKRLYEQNIPTQIFYIPSTILLILEDKTIK
GCISVEPYILGEFVKLSNNTKVVKTEYKATEYGLAYGHFSYEFSNHRDVVVDLQGWVTGNGKGLIYLTDP
QIHSVDQKVFTTNFGKRGIFYFFNNQHVECNEICHRLSLTRPSMEKP

Figure 11B

FIGURE 12   Sheet 23 of 31   601-1-098

FIGURE 12

HeEF-2_kinase>	1	LCD--ELIKIA QPFGR----E EC TKK SNFLHAQQWKGASN- RI ISP DR----DV
MHCK_B>	1	CT--ATL K EPVPFAE----- TLD S--------KSGASGR- IGKKPTPR--PS
Melanoma_kinase>	1	QLGLCAK EFL EMG------ VQCTWS---EHD LKS HI------ SLPE VNTWSSI TVLH CLRE
Kidney_kinase>	1	CRGRAAM Q L EMD------ VVSTWS---EDD LKP VE SSLPE VRTWHKI STVLH CLRE
Muscle_kinase>	1	GDK-- FGR B LRG GYGCE SQAKV YG--LEP FES RTC VSSLL FGPSSETSLVGRNYD TIQG
Heart_kinase>	1	GGR---- RGQ A LHF -EGVH STW HG--LMP FKP HAC VHNAIAYGTRNNDELIQRNYK AAQE
Lymphocyte_kinase>	1	AQ TI Y GDYLTVKKK-----RQ N WVHH H-------QEEILGR G KEQKGL---WHHFT
consensus	1	wt v imse G amRkafr l i g yviK y v y ed l

HeEF-2_kinase>	62	R ME L GEE RH PKQ--VV MQ CI E KD P-GKPL H-- E K I------- F RD N-IR
MHCK_B>	56	K MI K ADIQ SF PKK--I FLQSCV P D T-SSDLICG-A P E R --------F SN --ER
Melanoma_kinase>	74	QQ RA QLTFA QM KSI--PYS RF E YCH-SAGQ FA- ECT R D----EI PTN -LE
Kidney_kinase>	74	QQ RA QLIYT QV QTI--PYT RF VE YCH-SANQ LT- R T R D----EITPTN -LE
Muscle_kinase>	75	CK NM RE CKI AAEARAAPGFG E Y PANNIP AT- D GKPL S CSREWGCAEAPTASGS EAM
Heart_kinase>	73	CY NT YAKI AAEAQPLEGFG E P PENNIP AT- E R M SIRD ----KEINF RR EAG
Lymphocyte_kinase>	58	ER MI Q LVTE KRLYEQNIPTQ FY PSTI ILEDKTIKGCIS P E V LS TK--V KT YKAT
consensus	81	v lQ akkw fn kp dip ml iflv r f lE yi gef kynnn g v dt

HeEF-2_kinase>	130	LTPQ RSGHQ ET--------LY H ET--- T D DG VR AL FYS-A RI
MHCK_B>	124	NTPQ SNHQ HY HY --- VG I QK FEK DT-K AI
Melanoma_kinase>	145	IML R E N S IKA EKRSCDMV P ED KN RAK -H SC
Kidney_kinase>	145	LML R E N S IKP VKQSR MV P ED RRN IAK -H SC
Muscle_kinase>	154	QKCQT M SF A D---WK VT ALR--- YQGLKESCFPA-L DR ASS -Q AY
Heart_kinase>	150	QKCCT M K S A LAK---- YKGPK CSMT-F DQ KAL -Q KY
Lymphocyte_kinase>	132	SYGL G S SNHRD WVT NGKGLIY HS V--- QKVFTI KRGIFYF NNQ VE BI
consensus	161	afsHwtyeyt g llvvDlqG vg d lTDpqi t d g fg gnlg gm F H CN C

HeEF-2_kinase>	196	ES G APF
MHCK_B>	190	QY N QS
Melanoma_kinase>	216	K K PDR
Kidney_kinase>	216	K K PD
Muscle_kinase>	221	EL G TP
Heart_kinase>	217	G KS
Lymphocyte_kinase>	206	R S TRP
consensus	241	r l L i

PHYLOGENETIC TREE OF ALPHA-KINASES

Human eEF-2 k
C.elegans eEF-2 k
MHCK B
MHCK C
MHCK A
Trypanosoma k
Melanoma k
Kidney k
Heart k
Muscle k
Lymphocyte k

FIGURE 13

FIGURE 14

601-1-098(1:
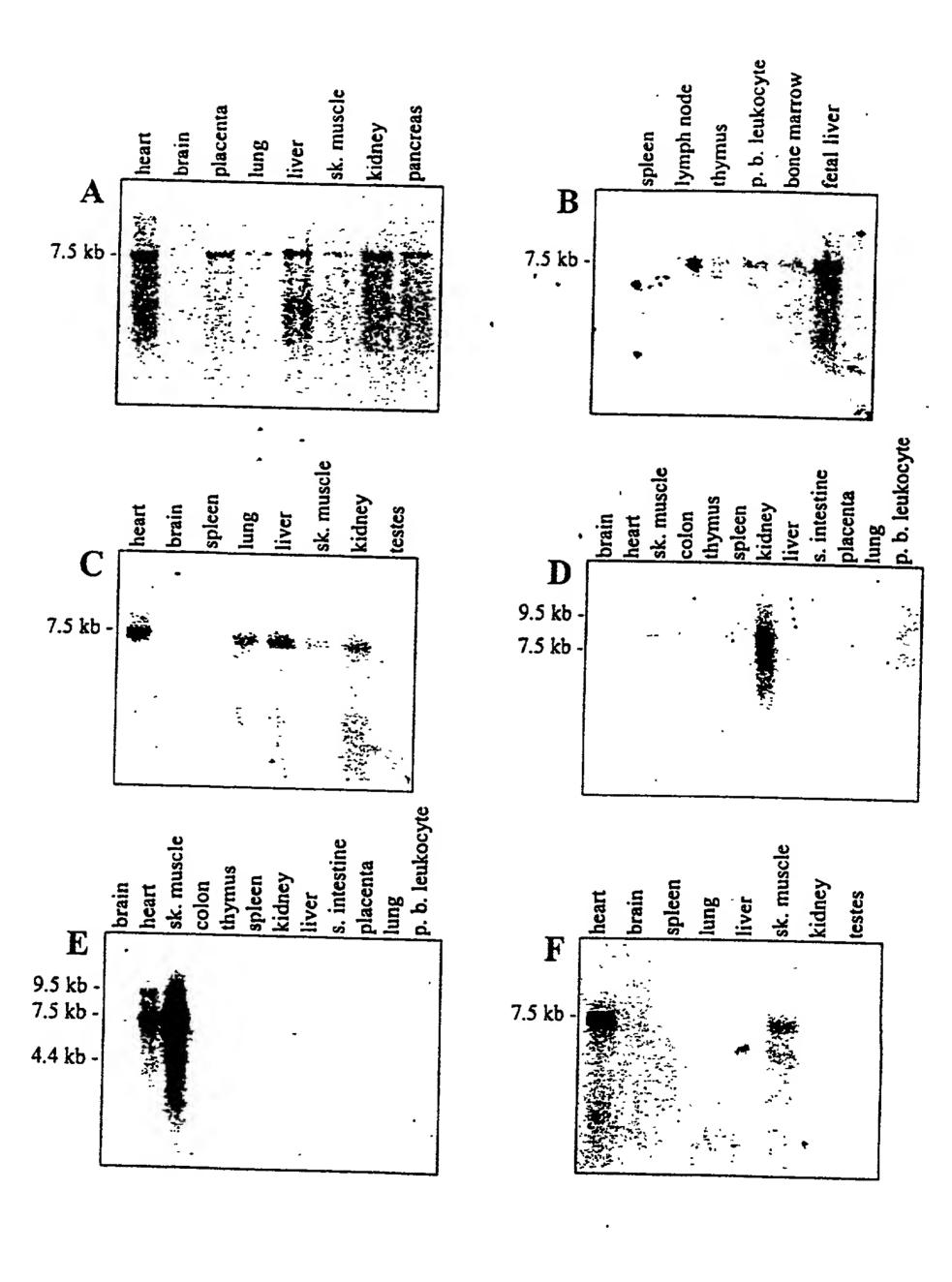
Time curve

melanoma kinase
catalytic domain.

| 0' | 5' | 10' | 20' | 30' | 60' | 120' |

FIGURE 15 Sheet 26 of 31 601-1-098 CIP

FIGURE 16   Sheet 27 of 31   601-1-098 CIP
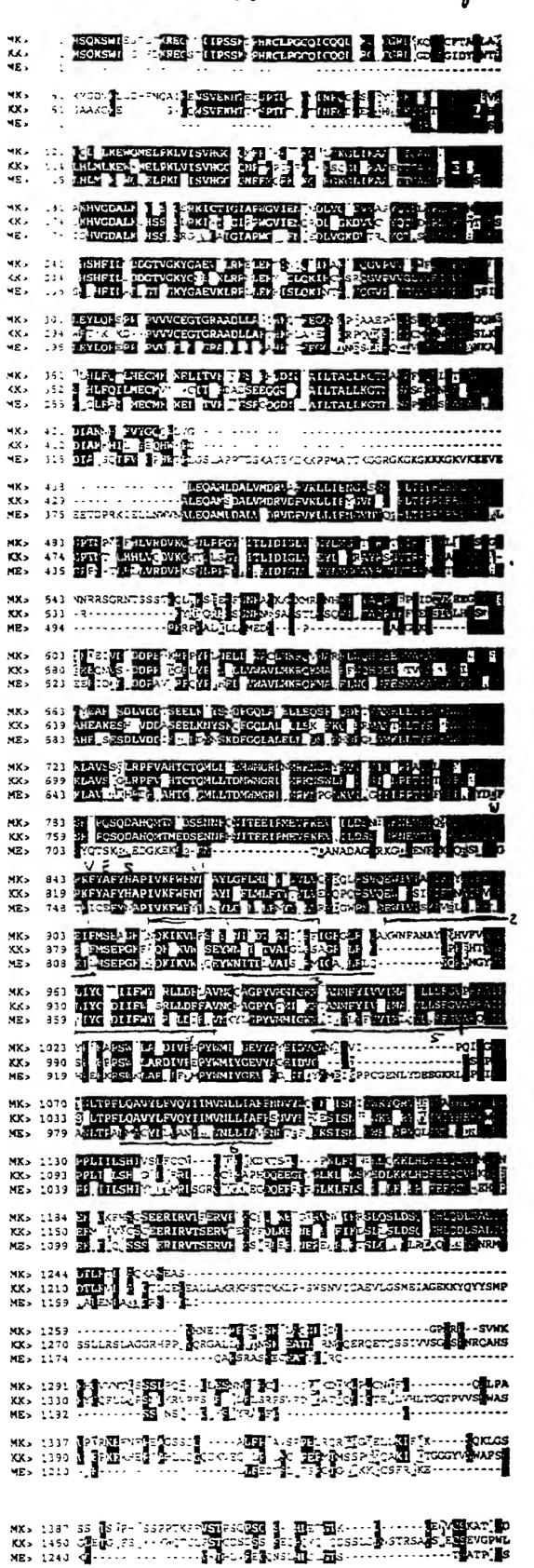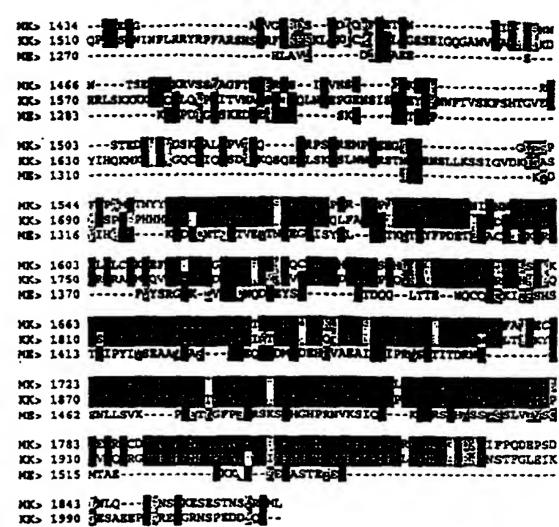
Figure 17

Figure 17

Figure 18

A

B

CeLTRPC3
CeLTRPC2
Melanoma kinase
Kidney kinase
Melastatin
LTRPC5
LTRPC6
LTRPC2
DmTRPC1
CeLTRPC1

TRP

catalytic domain

Figure 19A&B